Table 2, after "6TH repeat" insert – (SEQ ID NO: 16)--.

Page 67-74, delete the previously filed Sequence Listing and renumber the claim and abstract pages as 67-71.

REMARKS

Applicant submits this Amendment to delete the previously filed Sequence Listing and to insert required references to SEQ ID NOS of the Sequence Listing filed concurrently herewith. Applicant respectfully requests examination on the merits of this application.

Respectfully submitted,

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hybridized in a hybridization solution (5 x SSPE, 50% formamide, 5 x Denhardt's solution, 0.5% SDS, 100 ~ .tg/ml denatured DNA, 10% dextran sulfate) at 37°C, follow ~ d by washing under a condition of 1 x SSC, 1.0% SDS, 37°C (Sambrook, J. et al., Molecular Cloning, Cold Spring Harbor Laboratory Press (1989)).

As a result, cDNAs derived from the rat and the mouse were isolated. The nucleotide sequence of these cDNAs were determined using a conventional method, and the nucleotide sequence in turn was used to determine amino acid sequence. The estimated amino acid sequences of human, rat, and mouse cDNAs are shown by a one-letter code and are compared, as shown in the following Table 1. The polypeptides having these amino acid sequences were designated as gankyrin. The human gankyrin gene and the mouse gankyrin gene had a 90% homology on the base sequence level and a 93% homology on the amino acid sequence level. On the other hand, human gankyrin gene and the rat gankyrin gene had a 91% homology on the base sequence level and a 94% homology on the amino acid sequence level.

Table 1

Human	MEGCVSNLMVCNLAYSGKLEELKESILADKSLATRTDQDSRTALHWACSAGHTEIVEFLL
Mouse	MEGCVSNIMICNLAYSGKLDELKERILADKSLATRTDQDSRTALHWACSAGHTEIVEFLL
Rat	MEGCVSNLMVCNLAYNGKLDELKESILADKSLATRTDQDSRTALHWACSAGHTEIVEFLL
Human	QLGVPVNDKDDAGWSPLHIAASAGRDEIVKALLGKGAQVNAVNQNGCTPLHYAASKNRHE
Mouse	QLGVPVNDKDDAGWSPLHIAASAGRDEIVKALLVKGAHVNSVNQNGCTPLHYAASKNRHE
Rat	QLGVPVNEKDDAGWSPLHIAASAGRDEIVKALLIKGAQVNAVNQNGCTALHYAASKNRHE
Human	IAVMLLEGGANPDAKDHYEATAMHRAAAKGNLKMIHILLYYKASTNIQDTEGNTPLHLAC
Mouse	ISVMLLEGGANPDAKDHYDATAMHRAAAKGNLKMVHILLFYKASTNIQDTEGNTPLHLAC
Rat	IAVMLLEGGANPDAKNHYDATAMHRAAAKGNLKMVHILLFYKASYNIQDTEGNTPLHLAC
Human	DEERVEEAKLLVSQGASIYIENKEEKTPLQVAKGGLGLILKRMVEG (SEQ ID NO: 2)
Mouse	DEERVEEAKFLVTQGASIYIENKEEKTPLQVAKGGLGLILKRLAESEEASM (SEQ ID NO: 3)
Rat	DEERVEEAKLLVTQGASIYIENKEEKTPLQVAKGGLGLILKRIVESEEASM (SEQ ID NO: 5)

The nucleotide sequence of human gankyrin is shown

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in SEQ ID NO: 1 and the amino acid sequence thereof is shown in SEQ ID NO: 2. The nucleotide sequence of mouse gankyrin is shown in SEQ ID NO: 3 and the amino acid sequence thereof is shown in SEQ ID NO: 4. The nucleotide sequence of rat gankyrin is shown in SEQ ID NO: 5 and the amino acid sequence thereof is shown in SEQ ID NO: 6. In addition, it was estimated that in the amino acid sequences of gankyrins, the region from amino acid Met at position 1 to amino acid Leu at position 13 is a signal sequence.

The amino acid sequence of the human gankyrin polypeptide thus obtained had 5.5 ankyrin repeats (Lambert, S. et al., Proc. Nati. Acad. Sci. U.S.A. (1990) 87, 1730-1734). This is shown in the following Table 2.

Table 2

ANK consensus SEQ ID NO: 10	G TPLHLAAR GHVEVVKLLLD GADVNA TK A I SQ NNLDIAEV K NPD D V K T M R Q SI N E
1st repeat SEQ ID NO: 11	DSRTALHWACSAGHTEIVEFLLQLGVPVNDKDD
2nd repeat SEQ ID NO: 12	AGWSPLHIAASAGRDEIVKALLGKGAQVNAVNQ
3rd repeat SEQ ID NO: 13	NGCTPLHYAASKNRHEIAVMLLEGGANPDAKDH
4th repeat SEQ ID NO: 14	YEATAMHRAAAKGNLKMIHILLYYKASTNIQDT
5th repeat SEQ ID NO: 15	EGNTPLHLACDEERVEEAKLLVSQGASIYIENK
6th repeat SEQ ID NO: 16	EEKTPLQVAKGGLGLILKRMVEG

In this table, the upper 3 lines represent ankyrin sequences, and the bottom 6 lines represent ankyrin repeats in the amino acid sequence of the gankyrin polypeptide of the present invention.

Furthermore, figure 15 shows the site and the number of ankyrin repeats in various proteins.

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In order to determine the position of the gankyrin gene on the chromosome, fluorescence in situ hybridization was conducted. Thus, lymphocytes isolated from human blood were cultured in an minimum essential medium (MEM) supplemented with 10% fetal bovine serum and